Applicant: Masayuki Tsuchiya et al. Attorney's Docket No.: 14875-0144US1 / C1-A0230P-US

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Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

- (Currently amended) A method for isolating nucleic acid encoding an antibody that binds to an antigen of a lesional tissue, wherein the method comprises the steps of:
- (a) isolating a single lesional tissue-infiltrating B cell from a lesional tissue by a technique that comprises using laser microdissection (LMD) to excise a region comprising the B cell from a section of the lesional tissue, wherein the lesional tissue is selected from the group consisting of a cancer tissue, a solid tumor lesion tissue, an inflammatory disease lesion tissue, a lesion tissue generated by infectious pathogens, an autoimmune disease lesion tissue, and an artificially prepared lesion tissue; and
- (b) obtaining a polynucleotide encoding an antibody heavy chain and a polynucleotide encoding an antibody light chain of the isolated B cell in a method comprising purifying mRNA from the isolated B cell after addition of (i) carrier cells that do not express any antibody genes, or (ii) carrier RNAs that are not antibody-encoding transcripts, wherein the antibody heavy chain and light chain are [[is]] specific for an antigen of the lesional tissue.
 - 2. (Original) The method of claim 1, wherein the lesional tissue is a cancer tissue.
 - 3. (Canceled)
- (Previously presented) The method of claim 1, wherein step (b) comprises the step of amplifying a nucleic acid encoding an antibody variable region.

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5. - 8. (Canceled)

- 9. (Currently amended) A method for producing an antibody, wherein the method comprises the steps of:
- (a) isolating a single lesional tissue-infiltrating B cell from a lesional tissue by a technique that comprises using LMD to excise a region comprising the B cell from a section of the lesional tissue, wherein the lesional tissue is selected from the group consisting of a cancer tissue, a solid tumor lesion tissue, an inflammatory disease lesion tissue, a lesion tissue generated by infectious pathogens, an autoimmune disease lesion tissue, and an artificially prepared lesion tissue;
- (b) obtaining a polynucleotide encoding an antibody heavy chain and a polynucleotide encoding an antibody light chain of the isolated B cell in a method comprising purifying mRNA from the isolated B cell after addition of (i) carrier cells that do not express any antibody genes. or (ii) carrier RNAs that are not antibody-encoding transcripts;
 - (c) preparing one or more expression vectors comprising the polynucleotides;
- (d) transforming a host cell with the one or more expression vectors to obtain a transformed host cell expressing the polynucleotides;
 - (e) culturing the transformed host cell; and
- (f) recovering an antibody expressed by the transformed host cell, wherein the antibody binds to an antigen of the lesional tissue.
 - 10. 11. (Canceled)
- 12. (Previously presented) The antibody production method of claim 9, wherein the method further comprises the steps of:
 - (1) contacting the antibody obtained by the method of claim 9 with a test lesional tissue;
 - (2) detecting binding between the antibody and the test lesional tissue; and
 - (3) selecting the antibody if it binds to the test lesional tissue.

13.- 14. (Canceled)

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15. (Previously presented) The method of claim 1, wherein the method is repeated for twenty or fewer B cells.

 (Previously presented) The method of claim 1, wherein the method is repeated for five or fewer B cells.

17. (Previously presented) The method of claim 1, wherein the lesional tissue is removed from a patient by surgical excision.

18. (Previously presented) The method of claim 1, wherein the lesional tissue is frozen.

19. (Previously presented) The method of claim 1, wherein the lesional tissue is fixed.

20. (Previously presented) The method of claim 1, wherein the B cell is a human B cell.

21. (Previously presented) The method of claim 1, further comprising obtaining the sequence of a variable region of the antibody heavy chain or light chain.

22. (Canceled)

 (Previously presented) The method of claim 1, wherein the lesional tissue is an inflammatory disease lesion.

24. (Previously presented) The method of claim 1, wherein the lesional tissue is a lesion generated by an infectious pathogen.

25. (Previously presented) The method of claim 1, wherein the lesional tissue is an autoimmune disease lesion

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26. (Previously presented) The method of claim 1, wherein the lesional tissue is an artificially prepared lesion.

- 27. (Previously presented) The method of claim 2, wherein the cancer tissue is selected from the group consisting of breast, lung, liver, colon, pancreas, prostate, and skin cancer.
- 28. (Previously presented) The method of claim 12, wherein the test lesional tissue is the lesional tissue from which the B cell was isolated.
- 29. (Previously presented) The method of claim 12, wherein the test lesional tissue is from an individual different than the individual from whom the B cell was isolated.
- 30. (Currently amended) A method for isolating nucleic acid encoding an antibody that binds to an antigen of a lesional tissue, wherein the method comprises:
- (a) isolating a single lesional tissue-infiltrating B cell from a lesional tissue by a technique that comprises using LMD to excise a region comprising the B cell from a section of the lesional tissue, wherein the lesional tissue is selected from the group consisting of a cancer tissue, a solid tumor lesion tissue, an inflammatory disease lesion tissue, a lesion tissue generated by infectious pathogens, an autoimmune disease lesion tissue, and an artificially prepared lesion tissue;
- (b) obtaining a first polynucleotide encoding an antibody heavy chain and a second polynucleotide encoding an antibody light chain of the isolated B cell in a method comprising purifying mRNA from the isolated B cell after addition of (i) carrier cells that do not express any antibody genes, or (ii) carrier RNAs that are not antibody-encoding transcripts; and
- (c) repeating steps (a) and (b) at least once to obtain polynucleotides encoding antibody heavy chains and light chains of at least one more lesional tissue-infiltrating B cell from the lesional tissue, wherein the antibody binds to an antigen of the lesional tissue.

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31. (New) The method of claim 1, wherein step (b) of the method comprises purifying mRNA from the isolated B cell after addition of carrier RNAs that are not antibody-encoding

transcripts,

32. (New) The method of claim 1, wherein step (b) of the method comprises purifying

mRNA from the isolated B cell after addition of carrier cells that do not express any antibody

genes.

33. (New) The method of claim 9, wherein step (b) of the method comprises purifying

mRNA from the isolated B cell after addition of carrier RNAs that are not antibody-encoding

transcripts.

34. (New) The method of claim 9, wherein step (b) of the method comprises purifying

mRNA from the isolated B cell after addition of carrier cells that do not express any antibody

genes.

35. (New) The method of claim 30, wherein step (b) of the method comprises purifying

mRNA from the isolated B cell after addition of carrier RNAs that are not antibody-encoding

transcripts.

36. (New) The method of claim 30, wherein step (b) of the method comprises purifying

mRNA from the isolated B cell after addition of carrier cells that do not express any antibody

genes.